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# 3.0 Physical Properties: Subcategory PFC Amines

## 3.1 Melting Point

**MELTING POINT of class of compounds** – NOT RELEVANT

All materials in this class are in liquid state.

## 3.2 Boiling Point, 3.3 Relative Density, and 3.4 Vapor Pressure

Boiling point is measured based on ASTM D1120-65, "Boiling Point of Engine Antifreeze". The method for density measurement conforms to ASTM D4052-96, "Density and Relative Density of Liquids by Digital Density Meter".
Vapor Pressure measurements used ASTM E1719-97, "Vapor Pressure Measurement by Ebuilliometry".

| | | | Specification Median | Specification Median | Calculated Average |
|---|---|---|---|---|---|
| **Product** | **CAS#** | **Predominant Molecule** | **Boiling Point[1] (Centigrade)** | **Density[1] (kg/m3)** | **Vapor Pressure[2] (pascals)** |
| G | 338-83-0 | Perfluorotripropylamine | 128 | 1817 | 1,440 |
| Ha | 311-89-7 | Perfluorotributylamine | 155* | 1850* | 432* |
| $H_b$ | 311-89-7 | Perfluorotributylamine | 174 | 1860 | 192 |
| I | 338-84-1 | Perfluorotriamylamine | 215 | 1940 | 15 |
| J | 143356-32-5 | Perfluoro-N,N,N',N'-tetrapropyl hexanediamine | 253 | 1900 | <2 |

1. Manufacturing Plant QC test results on each Lot

2. Calculated average values were measured and extrapolated to STP (Standard Temperature & Pressure) using accepted values for constants A&B with the Clausius-Clapeyron equation.

* Verified, SMM Analytical Laboratory Report GID: 19159 dated July 16, 2001

## 3.5 Octanol/Water Partition Coefficients

Product **Ha**, CAS # 311-89-7, has been tested for octanol-water partitioning; the available data follow**.** Given the properties of PFCs, the likely ultimate fate of this class of compounds is release to the atmosphere, and modeling indicates partitioning to aquatic environments would be insignificant. Thus, octanol/water partitioning is insignificant to environmental risk assessment. 3M does not plan any additional testing on this property for these chemicals.

| | |
|---|---|
| **Test Substance:** | Test sample is product **Ha**. The production lot number was not noted. The purity of the substance cannot be verified to be 100%. The substance is a clear, colorless, odorless liquid. |
| **Method:** | 3M derived procedure using gas chromatography - 3M Commercial Chemicals Analytical group. |
| **GLP:** | No |
| **Year:** | 1981 |
| **Test procedure:** | The sample was prepared by mixing 25 uL of **Product Ha** with 100 mL of distilled water and shaking for 12 hours. A 50 mL aliquot was then shaken for 15 hours with 50 mL of prewater-saturated 99+% n-octanol. The mixture was allowed to stand for 2 hours. The n-octanol phase was analyzed directly, and the water phase was extracted with hexane and analyzed. Analysis was by gas chromatography. Distribution was determined by dividing the concentration in n-octanol by the concentration in water. |
| **Results:** | n-octanol concentration/water concentration = 557 |
| **Test Remarks:** | The test temperature was not recorded in the summary report. |
| **Conclusion:** | Though not conclusive, this study indicates that the octanol/water partition coefficient for **Product Ha** is 557. |
| **Data Quality:** | Klimisch ranking = 3. This study does not meet criteria for quality testing as temperature was not recorded |
| **Reference:** | 3M, Commercial Chemicals Analytical Request #17322 and Analytical Report #263 and #269. |

## 3.6 Water Solubility

Water solubility data are presented on Product **Ha**; the available data follows. While testing was conducted under informal R&D procedures, thus lacking full documentation, it is believed these results exemplify the low water solubility of this class of chemicals.

| | |
|---|---|
| **Test Substance:** | Test sample is **Product Ha**. The production lot number was not noted. The purity of the substance cannot be verified to be 100%. The substance is a clear, colorless, odorless liquid. |
| **Method:** | 3M derived procedure using gas chromatography - 3M Commercial Chemicals Analytical group. |
| **GLP:** | No |
| **Year:** | 1981 |
| **Test procedure:** | One sample consisted of 25 uL of **Product Ha** added to 100 mL of distilled water and shaken for 12 hours. Another sample was prepared by adding 5 uL of **Product Ha** to 1000 mL of distilled water and shaken for 12 hours. These samples were allowed to stand for 15 hours and then centrifuged. 25 mL aliquots of each were extracted with three consecutive 5 mL aliquots of hexane and the extracts were analyzed separately by gas chromatography. |
| **Results:** | Water solubility was indicated to be 0.68 ppm. |
| **Test Remarks:** | Detection limit for the method was 0.03 ppm. The test temperature was not recorded in the summary report. It is not disclosed if the samples were allowed to sit open to the environment or if they were closed during the 15-hour rest period. |
| **Conclusion:** | Though not conclusive, this study indicates that the solubility of the test substance is <1 ppm. Low water solubility is indicative of the class of compounds covered by CAS number 86508-42-1. |
| **Data Quality:** | Klimisch ranking = 3. This study does not meet criteria for quality testing. Proper documentation of test conditions was not followed. |

**Reference:** 3M, Commercial Chemicals Analytical Request #17322 and Analytical Report #263 and #269.

## 3.7 pH and pKa Values

**pH and pKa VALUES –** NOT RELEVANT

There is no water in any of these material so no ionization occurs.

## 3.8 Oxidation-Reduction Potential

**Oxidation-Reduction Potential –** NOT APPLICABLE

The standard oxidation-reduction potentials do not apply to PFCs. The materials are unaffected by electrochemical reactions and do not dissociate in aqueous media. They are essentially already fully oxidized and are unaffected by standard oxidizing agents such as permanganates, chromates, etc. The only known oxidation takes place only at high temperatures by thermal decomposition. Likewise, the materials are only reduced under extreme conditions, requiring reducing agents such as elemental sodium.

## 3.9 Adsorption/Desorption to Soil

**Adsorption/Desorption to Soil** - NOT APPLICABLE

As outlined in the explanation for how these chemicals are used, the predominant release of these chemicals will be to the atmosphere. Because of the volatility of these compounds, OECD methods do not apply.

# 4.0 Environmental Fate and Pathways: Subcategory PFC Amines

## 4.1 Photodegradation

Extensive research has addressed the photodegradation of this class of compounds. The following is information that was presented to the United States Environmental Protection Agency resulting in the successful elimination of this chemical class from regulation as VOCs based on their photochemical stability.

**Test Substance:** C5-C18 perfluorinated chemicals covered by CAS number 86508-42-1.

**Method:** Calculated

**GLP:** No

**Year:** 1990

**Overview:**

This overview combines both PFC alkane and amine data.

R. J. Cicerone[1] published theoretical calculations indicating that the perfluorochemical, carbon tetrafluoride, is essentially inert in the atmosphere. His calculations predicted an atmospheric lifetime of more than 10,000 years. In addressing reactions with hydroxyl radicals, Cicerone states: "Reactions of ground-state OH· with $CF_4$ are strongly endothermic and thus negligible." To support this statement, Cicerone presented the following candidate reactions between hydroxyl radical and $CF_4$ (Rx. 1. – Rx. 3.) with calculated enthalpies:

| Reaction | ?H298 (kcal/mole) | |
|---|---|---|
| $OH\cdot + CF_4 \rightarrow FO + CF_3H$ | +73.0 | Rx. 1. |
| $OH\cdot + CF_4 \rightarrow HOF + CF_3$ | +70.2 | Rx. 2. |
| $OH\cdot + CF_4 \rightarrow$ other products | +77 | Rx. 3. |

Extrapolation from $CF_4$ to other perfluoroalkanes is reasonably straightforward. Fabian, et al. quote the >10,000 year lifetime calculated by Cicerone and state: "… a similar lifetime can be assumed for C2F6…".[2]

Reactions 4., 5., and 6., given below, show that, at least in terms of hydroxyl radical reactions with perfluorocarbons, this is a reasonable extrapolation. Reaction 4. and 5. show that the fluorine radical (F·) is more reactive with hydrogen containing organic materials than the hydroxyl radical, while reaction 4. shows that reaction between the more reactive F· and a perfluorocarbon (RF) is very unfavored energetically.

| Reaction | ?H (kcal/mole) | |
|---|---|---|
| $RH + F\cdot \rightarrow R\cdot + HF$ | -34 | Rx. 4.[3] |
| $RH\cdot + OH\cdot \rightarrow R\cdot + H_2O$ | -13 | Rx. 5.[4] |
| $RF\cdot + F\cdot \rightarrow R\cdot + F_2$ | +68 | Rx. 6.[3] |

Expressed more graphically, mixing F· with ethane would yield an explosive reaction, but mixing F· radical with a perfluorocarbon, would lead to no reaction at all. One can conclude from the above that the reaction rate between a perfluoroalkane and OH· is much less than that between a OH· and ethane.

The most potentially reactive of this perfluorocarbon class, the perfluorinated tertiary amines and the quite analogous perfluorinated ethers, are similarly unreactive. This is supported by the following statement from Fluorine in Organic Chemistry: [5] "Perfluoro tertiary amines $(R_f)_3N$ are very inert systems and are more akin to perfluoroalkanes than amines." Ulmann's Encyclopedia of

Industrial Chemistry also addresses the inertness of perfluoroalkyl tertiary amines.[6] This article states:

> "The electron-withdrawing nature of the perfluoroalkyl substituents deprives the nitrogen atom of its basic character and reactivity. Fluorinated *tert*-amines do not form salts or complexes with strong acids and are not attacked by most oxidizing or reducing agents."

Studies conducted by 3M show that perfluoro tertiary amines don't react with fluorine radicals under room temperature conditions[7]. These studies offer further confirmation that perfluoro tertiary amines like perfluoroalkanes are extremely stable. The similar inertness of perfluoroethers is implicitly shown in a European patent application on a process for preparing perfluoroethers with elemental fluorine.[8] In this process, a perfluoroether used as a solvent for this reaction is later recovered, demonstrating the stability of the perfluoroether to fluorine radical.

Numerous published articles show that no degradation of perfluorocarbons is expected in the troposphere.[9-17] McElroy et al. investigated the atmospheric fate of various perfluorinated compounds including C6 to $C_{10}$ perfluoroalkanes. They concluded that perfluorocarbons do not react at significant rates with hydroxyl radicals and that such compounds will only degrade in the upper atmosphere through reactions with O(1D) yielding an approximate average atmospheric lifetime of 1,000 years. More recent work at MIT has shown that perfluoroalkanes do not react with 0(1D), at least not at rates comparable to those of CFCs. These newer findings suggests that reactions with 0(1D) in the stratosphere would not play a significant role in the degradation of perfluoroalkanes.

Ko et al. predict the photo- and oxidative-degradation rates of the perfluorochemical based on UV absorption spectra and assumed quantum yields.[10] They conclude that photodegradation would not occur in the troposphere. Calloway et al. further evaluate the UV absorption spectra of perfluoroalkanes and perfluoro-aromatic molecules.[11] This work shows that absorption spectra of perfluorocarbons occur at wave lengths too short to allow direct photodissociation in the troposphere. UV absorption maxima of perfluoroalkanes are generally below 190 nm. Most aromatic perfluorochemicals have absorption onsets below 260 to 280 nm, but some, such as perfluoronaphthalene, have absorption as high as 330 nm.

Yet another demonstration of the photochemical stability of perfluorochemicals is their use as inert solvents in a study reported by Chen et al. of the UV photolysis of other organic compounds.[12] Similarly, 3M has used liquid perfluoroalkanes and perfluoroethers as coolants for photochemical reactors, a use in which they receive intense exposure to UV light without photodegrading.

A very clear demonstration of the stability of saturated perfluorocarbons can be ascertained from the measurements by Dietz et al.[13] They measured the atmospheric concentrations of two fluorocarbons, perfluoromonomethylcyclohexane and perfluorodimethylcyclohexane. The bulk of these two fluorocarbons had been released to the atmosphere 30 to 40 years prior to Dietz's measurements, yet they were present in the atmosphere at near the cumulative concentration expected from their total worldwide production.

References:


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33. Sandorfy, C., UV Absorption of Fluorocarbons, Atmospheric Environment, Vol. 10, p343, 1976.
34. Yi Tang, Atmospheric Fate of Various Fluorochemicals, Thesis submitted to Department of Chemistry, Massachusetts Institute of Technology, 10, September, 1993.

**Conclusion:**

The class of compounds covered by CAS number 86508-42-1 are photochemically stable.

**Data Quality:** This information is considered reliable.

**Reference:**

Submission to THE UNITED STATES ENVIRONMENTAL PROTECTION AGENCY by THE MINNESOTA MINING AND MANUFACTURING COMPANY, *Request for the Exemption of Certain Perfluorocarbon Compounds From Regulation Under the Clean Air Act as Precursors to Tropospheric Ozone*, February 16, 1990.

## 4.2 Stability in Water

These compounds are highly volatile and insoluble. They are therefore not likely to partition to aquatic environments from the atmosphere. These compounds are extremely unlikely to undergo hydrolysis and testing is unnecessary.

## 4.3 Biodegradation

PFCs are not biodegradable. As an example, 3M presents data on Product **Ha.**

| | |
|---|---|
| **Test Substance:** | **Product Ha,** production lot number not noted. The purity of the substance cannot be verified to be 100%. The substance is a clear, colorless, odorless liquid. |
| **Method:** | 3M BOD/COD tests – method not recorded |
| **Test solutions:** | 3.0 g **Product Ha**/ 300 ml = 10,000 mg **Product Ha**/L |

| | |
|---|---|
| **Medium:** | BOD water inoculated at 6 mg/L with stale sewage from 3M's wastewater treatment plant in Cottage Grove, MN |
| **GLP:** | No |
| **Year:** | 1981 |
| **Results:** | BOD 5 days < 200 mg/kg<br>BOD 10 days < 200 mg/kg<br>BOD 20 days < 200 mg/kg |
| **Remarks:** | Water is not a likely environmental release media. The substance was tested in duplicate. The primary standard solution (glucose-glutamic acid) met requirements for biodegradation. No toxicity control was conducted. Testing was conducted well above the solubility limit of this material. |
| **Conclusion:** | The substance was not found to be biodegradable. This result is representative of the class of compounds covered by CAS number 86508-42-1. |
| **Data Quality:** | Klimisch ranking = 3 due to lack of a toxicity control. |
| **Reference:** | 3M, Environmental Laboratory – laboratory request number –7044 |

## 4.4 Fugacity

As outlined in the explanation for how these chemicals are used, the predominant release of these chemicals will be to the atmosphere. Calculated Henry's Law Constants for these compounds indicate that a release of the liquid material would result in a relatively rapid volatilization to the air. For this reason, fugacity modeling has been approached assuming 100% release to the atmosphere. Modeling for 3 compounds has been included to cover the range of chemicals, and was conducted utilizing the Level III Fugacity Model as part of the Syracuse Research Corporation EPISuite package available from the U.S. EPA. This modeling indicates that, once released to the atmosphere, the PFC amines are expected to stay in the atmosphere.

**Product I**

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : Pentanamine, 1,1,2,2,3,3,4,4,5,5,5-undecafluoro-N,N-
bis(undecafl
```

```
oropentyl)-
  Molecular Wt: 821.12
  Henry's LC  : 7.91e+006 atm-m3/mole (Henrywin program)
  Vapor Press : 0.014 mm Hg  (user-entered)

           Mass Amount    Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       96.7            1e+005       1000
   Water     0.00398         3.6e+003     0
   Soil      3.05            3.6e+003     0
   Sediment  0.209           1.44e+004    0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       2.97e-011    0.692       999         0.0692      99.9
   Water     3.92e-011    0.00079     0.00411     7.9e-005    0.000411
   Soil      2.25e-011    0.606       0           0.0606      0
   Sediment  6.95e-011    0.0104      0.00431     0.00104     0.000431

   Persistence Time: 103 hr
   Reaction Time:    7.89e+004 hr
   Advection Time:   103 hr
   Percent Reacted:  0.131
   Percent Advected: 99.9

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      1e+005
      Water:    3600
      Soil:     3600
      Sediment: 1.44e+004
        Biowin estimate: -2.955  (recalcitrant)

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

# 5.0 Ecotoxicity: Subcategory PFC Amines

## 5.1 Acute Toxicity to Fish

This class of chemicals presents no aquatic toxicity due to the lack of water solubility, as demonstrated in test data on several products.

| | |
|---|---|
| **Test Substance:** | **Product Ha**, production lot number 501. The purity of the substance cannot be verified to be 100%. The substance is a clear, colorless, odorless liquid. |

| | |
|---|---|
| **Method:** | Modeled after ASTM E729-80. Standard for conducting acute toxicity tests with fishes, macro-invertebrates, and amphibians. American Society for Testing and Materials, Philadelphia, PA 1980. |
| **Test Type:** | Acute Static |
| **Test Solutions:** | Well water used as vehicle. 2 control vessels and test vessels containing Product Ha concentrations of 10, 100, 1000, 2000, and 4000 mg/l (direct addition of individually measured weights). |
| **Test organism:** | Fathead minnow (*Pimephales promelas*) with average length of 3.0 cm and average weight of 0.251 grams. |
| **Exposure Period:** | 96 hours |
| **Analytical Monitoring:** | pH, dissolved oxygen, and temperature. All remained within acceptable parameters throughout the test. |
| **GLP:** | No |
| **Year:** | 1981 |
| **Results:** | $LC_{50}$ = > 1000 mg/l (Today, this would be termed an $LL_{50}$ = Median Lethal Loading.) |
| **Remarks:** | Water is not a likely environmental release medium. The substance is not soluble in water and formed a surface film on the water at the high concentrations. Exposures were therefore to saturated solutions. The loading factor for the test was 0.4 g/L utilizing 5 organisms per dose. |
| **Conclusion:** | No statistically significant mortality or other adverse effects occurred during this study. The 96-hr. $LC_{50}$ for fathead minnows therefore exceeds the solubility limit for the test substance. This result is representative of the class of compounds covered by CAS number 86508-42-1. |
| **Data Quality:** | Klimisch ranking = 2. This study meets most of the criteria for quality testing. Proper documentation of the test method and parameters was followed. However, no analysis of the actual test substance concentration was made, nor was there analytical characterization of the sample itself. |

| | |
|---|---|
| **Reference:** | 3M, Environmental Laboratory – laboratory request number 7044 |

* * *

| | |
|---|---|
| **Test Substance:** | **Product I**, production lot number 89. The substance is a clear, colorless, odorless liquid. The purity of the substance cannot be verified to be 100%. |
| **Method:** | Modeled after ASTM E729-80. Standard for conducting acute toxicity tests with fishes, macro-invertebrates, and amphibians. American Society for Testing and Materials, Philadelphia, PA 1980. |
| **Test Type:** | Acute Static |
| **Test solutions:** | Well water used as vehicle. 2 control vessels and 2 vessels containing 1000 mg/l of Product I (direct addition of individual weights). |
| **Test organism:** | Fathead minnow (*Pimephales promelas*) with average length of 2.9 cm and average weight of 0.19 grams. |
| **Exposure Period:** | 96 hours |
| **Analytical Monitoring:** | pH, dissolved oxygen, and temperature. All remained within acceptable parameters throughout the test. |
| **GLP:** | No |
| **Year:** | 1982 |
| **Results:** | $LC_{50}$ = > 1000 mg/l (Today, this would be termed an $LL_{50}$ = Median Lethal Loading.) |
| **Test Remarks:** | Water is not a likely environmental release medium. The substance is not soluble in water and remains as a separate phase on the tank bottom. Exposure was therefore to a saturated solution. The loading factor for the test was 0.19 g/L utilizing 30 organisms per dose. |
| **Conclusion:** | No adverse affects or mortality occurred during this study. The 96-hr. LC50 for fathead minnows therefore exceeds the solubility limit for the test substance. This |

result is representative of the class of compounds covered by CAS number 86508-42-1.

**Data Quality:** Klimisch ranking = 2. This study meets most of the criteria for quality testing. Proper documentation of the test method and parameters was followed. However, no analysis of the actual test substance concentration was made, nor was there proper analytical characterization of the sample itself.

**Reference:** 3M, Environmental Laboratory – laboratory request number 7981

## 5.2 Acute Toxicity to Aquatic Invertebrates

This class of chemicals presents no aquatic toxicity due to the lack of water solubility, as demonstrated in the tests described below.

**Test Substance:** **Product Hb**, production lot number 1053. The purity of the substance cannot be verified 100%. The substance is a clear, colorless liquid.

**Method:** Not given.

**Test Type:** Static Renewal

**Test solutions:** 1 control vessel and test vessels containing nominal substance concentrations of 4, 40, and 400 mg/l. Water source not described.

**Test organism:** Water Flea (*Daphnia magna*)

**Exposure Period:** 21 days

**Analytical Monitoring:** Temperature was recorded for all test concentrations. Control was monitored for DO saturation and pH. All were within acceptable limits..

**GLP:** No

**Year:** 1984

**Results:** 14-day $EC_{50}$ (Adult mortality) = > 400 mg/l
14-day $EC_{50}$ (Reproduction) = >400 mg/l
14-day NOEC (Reproduction) = 40 mg/l
14-day NOEC (Survival) = 400 mg/l

21-day $EC_{50}$ (Adult mortality) = > 400 mg/l
21-day $EC_{50}$ (Reproduction) = >400 mg/l
21-day NOEC (Reproduction) = 40 mg/l
21-day NOEC (Survival) = 400 mg/l

**Test Remarks:** Data for this study are averages of four replications for each treatment with five (5) daphnids per replicate. A total of twenty daphnids were used per treatment.

**Conclusion:** While water is not a likely environmental release media, the 21-day $EC_{50}$ for chronic effects towards *Daphnia magna* indicates FC-43 would not likely adversely affect the reproductive life cycle. This result is considered representative of the amine class of compounds covered by CAS number 86508-42-1.

**Reference:** 3M Company, Environmental Laboratory – laboratory request number B1362.

## 5.3 Acute Toxicity to Aquatic Plants

Testing to determine the toxicity of the class of compounds covered by CAS 86508-42-1 to algae or other aquatic plants has not been conducted. Since it is unlikely that the aquatic environment will be significantly exposed to these compounds based on their physical / chemical properties, and data on other phyla has been submitted, further testing is not necessary. 3M submits additional data on bacteria (*Photobacterium phosphoreum*) to support its position that these compounds would not exhibit significant aquatic toxicity.

**Test Substance:** **Product Ha**, production lot number 920124. The purity of the test substance cannot be verified to be 100%. The substance is a clear, colorless, odorless liquid.

**Method:** 3M EEF Method "Microtox® Toxicty Test procedure" as well as the Environmental Canada Biological Test Method: "Toxicity Test Using Luminescent Bacteria *(Photobacterium phosphoreum)*"

**Test solutions:** 3 control vessels and triplicate test vessels containing a saturated solution of the test substance in water. Test solutions were created by adding 100 mg test substance to 1 L deionized water, and allowing the solution to stir overnight. As the solubility of the test substance has been described as 0.68 mg/L, the actual concentration of the test substance in the stock solution was expected to be approximately 0.68 mg/L. An osmotic adjustment was

| | |
|---|---|
| | made using 0.9 g NaCl dissolved in 45 mL sample solution (2% NaCl solution). Sample solution had an initial pH of 5.3, and was adjusted to 5.92 with the addition of NaCl. The final appearance of the test solution was described as a "clear, colorless, odorless liquid". |
| **Test Type:** | Acute Toxicity |
| **Test organism:** | *Photobacterium phosphoreum* |
| **Exposure Period:** | 5, 15, and 30 minutes |
| **Analytical Monitoring:** | light readings |
| **GLP:** | No |
| **Year:** | 2003 |
| **Results:** | **100% saturated solution testing:**<br>5 minutes: Mean Normalised Light Loss = 0.3106<br>Mean Percent Light Loss = 23.70<br>15 minutes: Mean Normalised Light Loss = 0.3241<br>Mean Percent Light Loss = 24.48<br>30 minutes: Mean Normalised Light Loss = 0.2693<br>Mean Percent Light Loss = 21.22 |
| **Test Remarks:** | Due to the low solubility of this material the test concentration was reduced from the method specified target of 100mg/L to 0.68 mg/L (saturation point). This was achieved by adding excess test material to water and using constant stirring overnight. It was noted that some material "stuck" to the weighing pan and couldn't be washed into the test solution. |
| **Conclusion:** | The 30-minute $EC_{50}$ for *Photobacterium phosphoreum* was determined to be greater than the saturation point of the test substance. |
| **Data Quality:** | Klimisch ranking = 2. This study meets most criteria for quality testing. The concentration of the test substance in solution was not determined, and an assumption of saturation has been made. The purity of the substance is not stated. |

| | |
|---|---|
| **Reference:** | 3M, Environmental Laboratory – laboratory request number E03-0332. |

# 6.0 Mammalian Toxicity: Subcategory PFC Amines

## 6.1 Acute Toxicity

An acute inhalation toxicity study was performed to evaluate the effects of a single exposure to very high doses of a test material. A variety of observations are made during exposure and during the usual 2-week recovery period. Results are usually reported as mg/kg (oral toxicity) or as ppm or mg/m3 (inhalation). Occasionally, intraperitoneal studies are performed. These results are usually reported as mg/kg.

**Summary of Acute Toxicity Data:**

Acute oral and inhalation toxicity studies performed with Compound **Ha** did not induce lethality or toxicity in any study at any concentration tested. An extremely high dose intraperitoneal injection study performed with Compound **Ha** in the rat resulted in no lethality. Compound **Ha**, as representative of the class of PFCs, is considered "non-toxic" by inhalation exposure.

| | |
|---|---|
| **Title:** | An Acute Inhalation Toxicity Study of T-4502 (**Product Ha**) in the Rat. 1969. |
| **Test Article:** | (**Product Ha**, T-4502) |
| **Method/Guideline:** | Not specified |
| **GLP:** | N |
| **Year Study Performed:** | 1969 |
| **Species/Strain:** | Charles River Albino rats |
| **Sex:** | Males and Females |
| **No. of Animals/Sex/Dose:** | 7/sex/group |
| **Route of Administration:** | Inhalation |
| **Remarks:** | Fourteen albino rats (seven male and seven female) were exposed to vapor of **Product Ha** in a 70 liter Plexiglass chamber for a period of four hours. The nominal concentration was found to be 41 mg/L air. At the end of the exposure period, four rats were sacrificed (two male |

| | |
|---|---|
| | and two female) and the lung tissue was examined microscopically. The remaining ten animals were returned to their stock cages and observed for the following 14 days. |
| **Results:** | There were no deaths, untoward behavioral reactions or adverse body weight effects caused by the inhalation of the test material. Necropsy of all test animals did not reveal any gross pathological alterations. Microscopic examination of the lung tissue in four animals did not reveal any histopathological alterations. |
| **Conclusions:** | The compound did not induce toxicity by inhalation. |
| **Reference:** | 1969. *An Acute Inhalation Toxicity Study of Product Ha in the Rat.* IBT No. N7109, Industrial Bio-Test Laboratories, Inc. |
| **Remarks:** | Similar results were obtained in a previous study (T-4501 done in 1962 on **Product Hb**) on three species (rats, mice, and guinea pigs) with concentrations up to 17 mg/liter. |

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| **Title:** | **Product Ha** (T-2740CoC) Acute Oral Toxicity (LD50) Study in Rats. 1980. |
| **Test Article:** | Identity: T-2740CoC **Product Ha** |
| **Method/Guideline:** | Riker Test Method 605A |
| **GLP:** | No, but was audited by the QA group |
| **Year Study Performed:** | 1980 |
| **Species/Strain:** | Charles River Albino Rats |
| **Sex:** | Male and Female |
| **No. of Animals/Sex/Dose:** | 5/sex/dose |
| **Vehicle:** | None |
| **Route of Administration:** | Gavage |

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| **Remarks:** | The rats were administered the test article at a dosage level of 5,000 mg/kg, followed by a 14 day observation period. Initial and final body weights, mortalities and adverse reactions were recorded. Necropsies were performed at the end of the 14 day observation period. |
| **Results:** | LD50: >5,000 mg/kg. No untoward behavioral reactions or deaths occurred during the 14 day observation period and body weight gains were noted for all animals which survived the test period. Necropsies performed at termination of the study revealed no visible lesions. |
| **Conclusions:** | The compound can be considered practically non-toxic on an acute oral basis. |
| **Reference:** | 1980. *Product Ha Acute Oral Toxicity (LD50) Study in Rats.* Study No. T-2740CoC, Riker Safety Evaluation Laboratory, St. Paul, MN. |
| **Remarks:** | Similar study, except for 10 g/kg dose, conducted in 1972 (T-457) also resulted in no deaths and no significant gross findings on autopsy. |

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| **Title:** | An Acute Intraperitoneal Toxicity Study of T-4502 (**Product Ha**) in the Rat. |
| **Test Article:** | **Product Ha**, T4502 |
| **Method/Guideline:** | Not specified |
| **GLP:** | No, no QA/QC indicated |
| **Year Study Performed:** | 1969 |
| **Species/Strain:** | Charles River albino rats |
| **Sex:** | Male and Female |
| **No. of Animals/Sex/Dose:** | 2/sex/group |
| **Route of Administration:** | Intraperitoneal injection |

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| **Remarks:** | Undiluted **Product Ha** was administered by injection into the peritoneal cavity to three groups of four rats (2 male and 2 female) each. The dose groups were 15.4, 23.1, and 34.6 g/kg. |
| **Results:** | There were no deaths. Abnormal stance, hypoactivity, and muscular weakness was observed at all doses within 15 minutes of compound administration. Ruffled fur was also observed at the high dose level. Weight gains were normal. No lesions were observed at necropsy. Necropsy revealed clear fluid in the abdominal cavity of all animals; and white soft ovoid masses attached to the mesentery near the blood vessels and/or free floating in the cavity. Watery vacuoles also were found in the subcutaneous tissue of the ventral abdomen. |
| **Conclusions:** | The acute intraperitoneal LD50 for **Product Ha** is greater than 34.6 grams per kilogram of body weight. Therefore, this material may be considered to be practically non-toxic when administered intraperitoneally. |
| **Reference:** | 1969. *An Acute Intraperitoneal Toxicity Study of Product Ha in the Rat.* IBT No. A7108, Industrial Bio-Test Laboratories, Inc. |

## 6.2 Primary Eye and Skin Irritation

Primary eye and skin studies performed with Compound **Ha** resulted in no adverse effects. Compound **Ha**, as representative of the class of PFCs is considered "non-irritating" to the eyes and skin.

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| **Title:** | Eye and Skin Irritation Report on Sample T-1495. |
| **Test Article**: | (**Product Ha**, T-1495) |
| **pH of Test Article:** | Not applicable |
| **Method/Guideline:** | Described in Section 1500.42 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973. |
| **Test Type:** | *in vivo* |

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| **Species/Strain/Cell:** | Albino rabbit |
| **Sex:** | Not specified |
| **No. of Animals/Sex/Dose:** | 6/single dose |
| **Total dose:** | 0.1 ml, concentration not specified, total dose not specified |
| **Contact Time:** | 7 days |
| **Observation Period:** | 1hr, 24 hr, 48 hr, 72 hr, 5 and 7 days |
| **Scoring Method Used:** | Grading system outlined in the "Illustrated Guide for Grading Eye Irritation by Hazardous Substances." |
| **Remarks:** | One tenth of a milliliter (0.1 ml) of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to serve as controls. The test material was not washed from the eyes. |
| **Results:** | Irritation score of zero for all ocular tissues (cornea, iris, and conjunctivae) for all test animals at all observation periods. |
| **Conclusions:** | The subject material is not an ocular irritant. |
| **Reference:** | 1976. *Eye and Skin Irritation Report on Product Ha (T-1495)*. Primary Eye Irritation Study Report, May 21, 1976, Biosearch, Inc. |
| **Other:** | Similar study done in 1969 (T-4953) on FC-43 (also referred to as **Product Hb**), Lot 137 concluded test material was practically non-irritating to the eye. |

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| **Title:** | Eye and Skin Irritation Report on Sample T-1495. 1976. |
| **Test Article**: | (**Product Ha**, Sample T-1495) |
| **pH of Test Material:** | Not specified |

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|---|---|
| **Method/Guideline:** | Described in Section 1500.41 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973. |
| **Test Type:** | *in vivo* |
| **Species/Strain/Cell Type:** | Rabbits/ albino |
| **Sex:** | Not specified |
| **No. of Animals/Sex/Dose:** | 6 total |
| **Total Dose:** | 0.5 ml, concentration not specified; total dose not specified |
| **Vehicle:** | None specified |

**Length of Time Test Material is in Contact with Animal/Cell:** 72 hr

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| **Grading Scale:** | Separate scores for erythema formation and edema formation are summed. The Draize method of scoring was employed. |
| **Remarks:** | Six albino rabbits had their hair clipped over a wide area and five tenths of one milliliter (0.5 ml) of test material was placed on abraded and intact prepared test sites on the same rabbit, then covered with gauze patches. An impervious material was wrapped snugly around the trunks of the animals to hold the patches in place. After 24 hours and 72 hours the coverings were removed and the degree of erythema and edema was recorded according to a standardized scale. |
| **Results:** | In all cases it is reported the primary skin irritation scores were 0; which indicates no reddening or swelling detected. |
| **Primary Irritation Score:** | 0.0 |
| **Remarks:** | No |
| **Conclusions:** | The subject material would not be classified as a primary irritant to albino rabbits. |

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| **References**: | 1976. *Eye and Skin Irritation Report on Product Ha (T-1495).* Primary Skin Irritation Study Report, May 21, 1976, Biosearch, Inc. |
| **Other:** | Similar study done in 1969 (T-4953) on **Product Hb**, Lot 137 concluded test material was non-irritating to the skin. |

## 6.3 Genotoxicity

Two reverse mutation assays are presented as representative of the PFC class. Both utilized the *Salmonella typhimurium* test system (Ames assay). For Compound **H**, cytotoxicity was reported at the highest dose tested, suggesting that the test system could be adequately dosed. No evidence of mutation was reported in the assay with Compound **H**. Although forward mutation and chromosome aberration studies have not been performed, the chemical and physical properties of the class suggest that there is no reason to believe that effects would be observed in these assays. Therefore, 3M does not propose to do these tests.

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| **Title:** | Mutagenicity Evaluation of T-2007 CoC. 1978. |
| **Test Article**: | (T-2007CoC, **Product Ha**) |
| **Method/Guideline:** | Ames et al., Mutation Research 31:347, 1975 |
| **Test Type:** | Reverse mutation, with and without activation |
| **Test system:** | Bacterial |
| **GLP:** | No, but SOP's listed |
| **Year Study Performed:** | 1978 |
| **Cell-Type/Line:** | Salmonella typhimurium strains TA1535, TA100, TA98, TA1537, TA1538, and Saccharomyces cerevisiae strain D4 with and without activation. |
| **Metabolic Activation:** | S9 liver homogenate from Aroclor 1254 induced Sprague-Dawley rats |
| **Concentrations Tested:** | 10 ul/plate, 25 ul/plate, 50 ul/plate, 100 ul/plate with and without activation. |
| **Statistical Methods Used:** | None |
| **Remarks:** | Spot test procedure used. |

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| **Results:** | The test article was not genotoxic when tested either with or without metabolic activation. Cytotoxicity was noted at the highest dose. The low dose in all cases was below a concentration that demonstrated any toxic effect. There were no test-specific confounding factors. Mutation frequencies were within the range of the vehicle controls. |
| **Conclusions:** | The test article was considered non-mutagenic under the study conditions utilized. |
| **Reference:** | Mutagenicity Evaluation of T-2007 CoC, Final Report. LBI Project No. 20838, January, 1978, Litton Bionetics, Inc. |

## 6.4 Repeat Dose Toxicity

Compound **Hb** exhibited low toxicity in a six-week inhalation study.

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| **Title:** | Subacute Inhalation Study in Rats on T-1549 (**Product Hb**) |
| **Test Article:** | (**Product Hb**, T-1549). Purity |
| **Method/Guideline:** | Not specified. |
| **Study Duration:** | 30 Days |
| **GLP:** | No |
| **Year Study Performed:** | 1977 |
| **Species/Strain:** | Rats/Sprague-Dawley from Charles River |
| **Sex:** | Both |
| **Number per Dose Group:** | 26 exposed (16 males and 10 females)/16 controls (11 males and 5 females) |
| **Route of Administration:** | Inhalation |
| **Doses and Frequency:** | Saturated atmosphere for seven hours per day, five days per week, for a total of 30 exposures. Concentration |

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| | expressed as mls T-1549 used per cubic meter total air volume flowed through the system (average 7.28 ml/$m^3$). |
| **Post-Observation Period**: | none, necropsy done at end of experiment |
| **Statistical Methods Used:** | t-test |
| **Remarks:** | Hematology, clinical chemistry, and histopathology done on 5 each of test males and females, and 3 each of control males and females. |
| **Results:** | A 30-day vapor inhalation study with the test material was conducted wherein rats were exposed to an atmosphere saturated with the test material for 7 hours a day, 5 days per week, for a total of 30 exposures. The average nominal chamber concentration of the test material was 13,382 mg/m. No deaths occurred during the exposure period. No significant differences in gross pathology, lunch and liver histopathology, blood chemistry, or hematology were observed between the control and test groups. |
| **Conclusions:** | The study indicates that the subacute inhalation toxicity of the test material is very low. |
| **Reference:** | 1977. *Report on the 30 day saturated vapor inhalation study on T-1549.* Report No. 3, Laboratory No. R16, Toxicology Research Laboratory, University of California, San Francisco. |

## 6.5 Reproductive Toxicity

As detailed earlier, PFCs are both chemically and biologically unreactive. Due to their high volatility and lack of solubility in biological media, no toxicity is attributed to these materials even at very high doses. In fact, perfluorochemicals structurally similar to those discussed have been used to "rescue" respiratory function in premature infants (1-9).

As evidenced by the human health and environmental toxicity endpoints that have been investigated to date, the materials within this class are all exceedingly low in toxicity. This class of materials is among the least toxic compounds known. The same physical/chemical properties that dictate the mechanisms of biological interaction in the studies conducted to date would also dictate the result of any longer term studies or studies intended to investigate other endpoints such as reproductive toxicity. On this basis, and in the interest of animal welfare, it has never been deemed prudent to pursue any further toxicological investigations with this

class of materials. Accordingly, 3M proposes to rely on existing data for other endpoints and will not undertake a reproductive study.

References:

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2: Merz U, Klosterhalfen B, Kellinghaus M, Peschgens T, Pluschke S, Hoernchen H. *Effects of single and multiple doses of perfluorocarbon in comparison with continuous partial liquid ventilation on gas exchange and lung pathology in newborn surfactant-depleted pigs.* Crit Care Med. 2001 Mar;29(3):645-51. PMID: 11373437 [PubMed - indexed for MEDLINE]

3: Davies MW, Dunster KR. *The effect of perfluorocarbon vapour on the measurement of respiratory tidal volume during partial liquid ventilation.* Physiol Meas. 2000 Aug;21(3):N23-30. PMID: 10984211 [PubMed - indexed for MEDLINE]

4: Merz U, Kellinghaus M, Hausler M, Pakrawan N, Klosterhalfen B, Hornchen H. *Partial liquid ventilation with surfactant: effects on gas exchange and lung pathology in surfactant-depleted piglets.* Intensive Care Med. 2000 Jan;26(1):109-16. PMID: 10663291 [PubMed - indexed for MEDLINE]

5: Nader ND, Knight PR, Davidson BA, Safaee SS, Steinhorn DM. *Systemic perfluorocarbons suppress the acute lung inflammation after gastric acid aspiration in rats.* Anesth Analg. 2000 Feb;90(2):356-61. PMID: 10648321 [PubMed - indexed for MEDLINE]

6: Burns MJ, Dickson EW, Sivilotti ML, Hocker M, Porcaro WA. *Enhanced mortality from perfluorocarbon administration in a rat model of kerosene aspiration.* J Toxicol Clin Toxicol. 1999;37(7):855-9. PMID: 10630269 [PubMed - indexed for MEDLINE]

7: Sajan I, Scannapieco FA, Fuhrman BP, Steinhorn DM. *The risk of nosocomial pneumonia is not increased during partial liquid ventilation.* Crit Care Med. 1999 Dec;27(12):2741-7. PMID: 10628620 [PubMed - indexed for MEDLINE]

8: Kuo CY, Hsueh C, Wang CR. *Liquid ventilation for treatment of meconium aspiration syndrome in a piglet model.* J Formos Med Assoc. 1998 Jun;97(6):392-9. PMID: 9650467 [PubMed - indexed for MEDLINE]

9: Dickson EW, Heard SO, Chu B, Fraire A, Brueggemann AB, Doern GV. *Partial liquid ventilation with perfluorocarbon in the treatment of rats with lethal pneumococcal pneumonia.* Anesthesiology. 1998 Jan;88(1):218-23. PMID: 9447875 [PubMed - indexed for MEDLINE]

## 6.7 Development and Teratogenicity Toxicity

As detailed earlier (1.3 Metabolism/Toxicology Summary), PFCs are characterized as being both chemically and biologically unreactive. Due to their high volatility and lack of solubility in biological media, no toxicity is attributed to these materials even at very high doses. In fact, perfluorochemicals structurally similar to those discussed have been used to "rescue" respiratory function in premature infants.

As evidenced by the human health and environmental toxicity endpoints that have been investigated to date, the materials within this class are all exceedingly low in toxicity. This class of materials is among the least toxic compounds known. The same physical/chemical properties that dictate the mechanisms of biological interaction in the studies conducted to date would also dictate the result of any longer term studies or studies intended to investigate other endpoints such as developmental toxicity. On this basis, and in the interest of animal welfare, it has never been deemed prudent to pursue any further toxicological investigations with this class of materials. Therefore 3M will not conduct developmental testing.